REMARKS

Status of Claims and Amendment

Claims 25-27 have been amended. New claims 33 and 34 have been added. Claims 1-24 and 29-32 have been canceled. Claims 25-28, 33, and 34 are all the claims pending in the application. Claims 7-19 and 25-29 are rejected.

Claim 25 has been amended to even further clarify that the antigen in a sample may be detected by an antibody "which binds to a peptide consisting of the amino acid sequence of SEQ ID NO:1." Support for the amendment to claim 25 may be found at least at page 2, lines 7-9 and lines 23-24 of the specification.

Claims 26 and 27 have been amended to replace "represented by" with "of" as suggested by the Examiner.

Claims 25-27 have been amended to remove quotation marks in response to objections to the claims.

Support for new claims 33 and 34 may be found at least at page 42, Example 8 of the specification.

No new matter is added.

Claim of Priority

Applicants thank the Examiner for acknowledgement of Applicants' claim of priority to Japanese Application No. 2002-213040 filed July 22, 2002, and Japanese Application No. 2003-70932 filed March 14, 2003, as well as receipt of copies of the priority documents.

Information Disclosure Statements

Applicants thank the Examiner for acknowledgement of the Information Disclosure Statement filed January 24, 2005, by returning a signed and initialed copy of the PTO Form SB/08 submitted therewith.

Although the International Search report dated September 2, 2003 was crossed out, the Examiner indicated that such document has been considered.

However, the Examiner has crossed out and not considered Hirata *et al.*, Proten Nucleic Acid and Enzyme, 46(4): 575-581 (2001). The Examiner requests a translation be provided.

Applicants submit that no translation has been reduced to writing to be available to Applicants or to be in Applicants' possession. Further, since the document was cited in an International Search Report and Applicants submitted an English translation of that part of the Search Report indicating the degree of relevance of Hirata *et al.*, Applicants respectfully request that the Examiner consider the document pursuant to M.P.E.P. §609.04(a).

Response To Claim Objections

Claims 7-18 and 25-27 are objected to by the Examiner because of the (1) quotation marks in claims 7-18 and 25-27, (2) claims 7 and 25 are dependent on a non-elected claim and should be written as independent claims, and (3) the phrase "represented by" in claims 7, 8, 10-12, 15, 16, 26 and 27 should be replaced with "of" for better clarity.

With regard to (1) and (3), Applicants have amended the claims to delete the quotation marks and replaced "represented by" with "of."

With regard to (2), Applicants have canceled claim 7 and amended 25 to be an independent claim.

Withdrawal of the grounds of objection is respectfully requested.

Response To Claim Rejections Under 35 U.S.C. § 103(a)

Claims 7-19 and 25-29 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ailsa Campbell (Monoclonal Antibody and Immunosensor Technology, Elsevier, p. 51-96; "Campbell I") and Ailsa Campbell (Monoclonal Antibody Technology, p. 1-31 (1984); "Campbell II") in view of Swierko et al (J. Med. Microbiol. vol. 49, p. 127-138, 2000, IDS reference).

The Office Action asserts that Campbell II teaches an immunoassay system using an antigen-antibody complex. Specifically, the Office Action asserts that Campbell II teaches attachment of an antigen to a solid support, use of a labeled antibody and secondary antibody, solid phase assays, and ELISA for bacterial or cellular antigens.

Campbell I is asserted by the Office Action for teaching that monoclonal antibodies are useful for therapeutic, diagnostic, and preparative and basic research, and that it is "customary" for one of ordinary skill in the art to make monoclonal antibodies.

The Office Action appears to acknowledge that Campbell I and Campbell II do not teach use of SEQ ID NO:1 or an antibody that binds to SEQ ID NO:1.

Swierko is cited by the Office Action for teaching that SEQ ID NO:1 is derived from human CAP18 and that $CAP18_{109-135}$ is clinically important for its LPS neutralizing domain and its antimicrobial domain. In addition, the Office Action asserts that Swierko teaches that Proteus bacteria causes pneumonia and the LPS from Proteus is endotoxic, but that treatment of Proteus LPS with $CAP18_{109-135}$ weakens the endotoxicity of Proteus.

The Office Action concludes that one of ordinary skill in the art would have been motivated to make an antibody to SEQ ID NO:1 and use it in the various immunological assays

of Campbell I and II to arrive at the present invention because using an antigen-antibody interaction in an immunoassay provides a diagnostic tool to detect LPS/CAP18 bacterial infection and immunoassays are known in the art. Also, the Office Action asserts that making monoclonal antibodies to a protein of interest is useful as an immunochemical tool.

Initially, Applicants note that this is an improper obviousness rejection because the Office Action has failed to provide any evidence that the primary reference, Campbell I, upon which the Office Action has based the entire rejection, is "prior art." There is no indication that Campbell I was published before the claimed invention. Although Campbell I is indicated on the PTO FORM-892 to have been published in 1991, there is no such documentation attached to Campbell I to support this publication date.

Nevertheless, Applicants will address the rejection on the merits because Applicants believe the Office Action has failed to establish a *prima facie* case of obviousness for at least the following reasons.

First, Applicants note that to establish a *prima facie* case of obviousness, "the prior art reference (or references when combined) must teach or suggest all of the claim limitations." M.P.E.P. §2143.

As acknowledged by the Office Action, neither Campbell I nor Campbell II teaches or suggests the use of the claimed amino acid sequence of SEQ ID NO:1 or an antibody that binds to SEQ ID NO:1. For that matter, neither Campbell I nor Campbell II teaches or suggests the amino acid sequence of SEQ ID NO:1 or any amino acid sequence.

Campbell I provides a mere general discussion of the assay requirements for screening monoclonal antibodies. In particular, Campbell I discusses the use of ELISA which is a method well-known to those of ordinary skill in the art. The general disclosure of Campbell I provides

no specific teaching or suggestion to detect a peptide comprising SEQ ID NO:1 in a sample using an antibody that binds to SEQ ID NO:1.

Similarly, Campbell II provides nothing further to the disclosure of Campbell I because Campbell II merely provides a general discussion of the general properties and applications of monoclonal antibodies. Campbell II is "essentially a laboratory manual based on the protocols and general advice" (see 1st sentence of the "Preface" of Campbell II) that was available to one of ordinary skill in the art in 1984 on monoclonal antibody production.

Accordingly, Campbell I and Campbell II merely disclose an immunoassay system using an antigen-antibody complex, especially general techniques of solid phase assays and ELISA for bacterial or cellular antigens and their general use.

Swierko does not cure the deficiencies of Campbell I and Campbell II. Although Swierko discloses a $CAP18_{109-135}$ which is similar to the claimed SEQ ID NO:1, Swierko is directed to examining the biological activities of lipopolysaccharides (LPS) and lipid A from Proteus bacterial strains. (See Abstract, 2nd sentence of Swierko). Swierko discloses that Proteus mirabilis causes pneumonia (page 127, 1st column, lines 1-5 of Swierko) and that $CAP18_{109-135}$ has the ability to neutralize LPS endotoxicity (sentence bridging pages 133-134 of Swierko).

However, Swierzko does not disclose an antibody bound to $CAP18_{109-135}$. Also, Swierzko does not disclose that bacterial pneumonia can be diagnosed by assaying $CAP18_{109-135}$ using the antibody. Particularly, Swierzko neither teaches nor suggests the concentration of CAP18 in the sputum is increased in patients with bacterial pneumonia, and that bacterial pneumonia can be detected by an assaying method using the antibody bound to $CAP18_{109-135}$.

Thus, there is nothing in Swierko that teaches or suggests a method of assaying or detecting an amino acid sequence of $CAP18_{109-135}$ in a sample or an antibody that binds to $CAP18_{109-135}$.

Second, the disclosure in Campbell I and Campbell II of assays for screening and producing monoclonal antibodies, and in Swierko of $CAP18_{109-135}$ does not teach or suggest the claimed method if the references do not suggest the desirability of such a modification. M.P.E.P. § 2144.08.

One of ordinary skill in the art would not have been motivated to combine Swierko with the general teachings of Campbell I and Campbell II, because one of ordinary skill in the art at the time the invention was made would not have surmised that the combination would result in the claimed invention. In the present case, neither Campbell I nor Campbell II teaches or suggests SEQ ID NO:1 or an antibody that binds to SEQ ID NO:1 despite the general discussion regarding methods of screening and producing monoclonal antibodies. Swierko does not cure this deficiency because although Swierko discloses $CAP18_{109-135}$, Swierko does not disclose detection of $CAP18_{109-135}$ in a sample using an antibody that binds to $CAP18_{109-135}$. To the contrary, Swierko at most discloses the use of $CAP18_{109-135}$ to inhibit proteus bacterium endotoxicity. Also, contrary to the Office Action's assertions at page 4 of the Office Action, that "Proteus [causes] pneumonia", inhibition of proteus bacterium endotoxicity is different from detecting bacterial pneumonia, because proteus bacterium is known in the art to be a pathogen responsible for human urinary tract infections, and not pneumonia.

Further, one of ordinary skill in the art would <u>not</u> have expected SEQ ID NO:1 to be immunogenic because Swierko only discloses the use of $CAP18_{109-135}$ to inhibit or "neutralize LPS endotoxicity" (see sentence bridging pages 133-134 of Swierko) by binding to Proteus LPS.

Also, Swierko discloses that $CAP18_{109-135}$ " alone did not induce any detectable NO production in [mouse macrophage-like] J774.1 cells" (see page 130, 2nd column, lines 4-8 of Swierko).

In the presently claimed method, bacterial pneumonia may be detected by assaying CAP18 or a partial peptide of CAP18 (SEQ ID NO: 1), instead of assaying bacteria-derived LPS. Accordingly, because the solid phase assays and ELISA for bacterial or cellular antigens are generally disclosed in Campbell I and Campbell II,[1] one of ordinary skill in the art would have expected that bacterial infection may be diagnosed by assaying LPS even if Swierzko merely discloses that the LPS neutralizing activity of CAP18 (leading to therapeutic effect) is considered. Therefore, one of ordinary skill would not have expected that the bacterial or cellular antigens of Campbell I and Campbell II may be replaced with the $CAP18_{109-135}$ of Swierzko for diagnosing bacterial pneumonia. Also, one of ordinary skill in the art would not have expected that bacterial pneumonia can be detected by assaying CAP18 or a partial peptide of CAP18.

Thus, even if Campbell I and Campbell II are combined with Swierzko, the presently claimed invention would not have been obtained or expected by one of ordinary skill in the art.

Furthermore, in the diagnosis of pneumonia, the detection is usually carried out by using a chest X-ray. The sensitivity against antibacterial agents is confirmed by culturing the sputum. The presence of infection or inflammation is confirmed by a blood test.

[1] Since the antigens are bacterial or cellular antigens *per se*.

However, X-rays may be misleading, because other problems, such as lung scarring and congestive heart failure, can mimic pneumonia on X-ray, and sputum cultures generally take at least two to three days (see Wikipedia; Diagnosis of Pneumonia which is submitted herewith)[2].

In contrast, bacterial pneumonia can be simply and precisely diagnosed using the presently claimed method by assaying CAP18 or a partial peptide of CAP18 using the antibody which binds to a partial peptide of CAP18 represented by SEQ ID NO:1.

Claims 7-19 and 29 have been canceled. Accordingly, the rejection with regard to these claims is rendered moot.

Reconsideration and withdrawal of the rejection under § 103(a) is respectfully requested.

[2] In accordance with M.P.E.P. 609(c), the documents cited herein in support of Applicants' remarks are being submitted as evidence directed to an issue raised in the Official Action, and no fee pursuant to 37 C.F.R. 1.97 or 1.98, or citation on a FORM PTO/SB/08 or PTO-1449 is believed to be necessary.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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Date: September 12, 2008